UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,132	06/15/2001	Peter Richard Reeves	6433/80968	7192

7590 07/01/2003

Welsh & Katz
22nd Floor
120 South Riverside Plaza
Chicago, IL 60606-3913

EXAMINER	
MYERS, CARLA J	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/701,132	REEVES ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. The Sequence Listing filed April 8, 2003 has not been entered because the disk filed did not contain a sequence listing, as indicated in the attached Raw Sequence Listing Error Report. The previously submitted sequence listing has been used to examine the present application. However, because this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2), Applicants must comply with the requirements of 37 CFR 1.821-1.825 in response to this Office action. In particular, Applicant is required to submit a new CRF copy of the Sequence Listing and a letter stating that the content of the paper and computer readable copies are the same.

2. Applicant's election with traverse of SEQ ID NO: 13 in the response of April 8, 2003 is acknowledged. Accordingly, claims 3-6 and 30-31 have been examined with respect to SEQ ID NO: 13; claims 12-13 and 16-17 have been examined with respect to claim 56; claim 20 has been examined with respect to SEQ ID NO: 57. The traversal is on the ground(s) that there is a special technical feature linking the claimed invention in that the claimed nucleic acids are capable of identifying an H serotype of E. coli other than the H1, H7, H12 and H48 type strains. This is not found to be persuasive because the common structure shared by the claims is that the claims are drawn to nucleic acids encoding all or part of an E. coli flagellin protein. It is acknowledged that Applicants written their claims so as to exclude nucleic acids encoding flagellin proteins from the E. coli strains H1, H7, H12, and H48 because these nucleic acids are taught in the prior art. However, the technical feature that links the claimed invention is not all E. coli flagellin nucleic acids except those taught in the prior art. If one considered that the technical feature of the

invention was the strain of E. coli to which the nucleic acid hybridized, then the claimed sequences would not share a technical feature since each of the claimed nucleic acids hybridizes to nucleic acids from different strains of E. coli. For example, SEQ ID NO: 7 hybridizes to nucleic acids of strain H5 and SEQ ID NO: 8 hybridizes to nucleic acids of strain H6. Accordingly, the overall technical feature linking the claimed invention is the structural and functional property of a nucleic acid that encodes a flagellin protein. This technical feature was taught in the prior art and thereby does not constitute a special technical feature.

The requirement is still deemed proper and is therefore made FINAL.

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

4. Claims 1-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids consisting of SEQ ID NO: 1-68 and primers consisting of 10 to 20 nucleotide fragments of SEQ ID NO: 1 to 68 or consisting of the specific nucleotide positions of SEQ ID NO: 56 set forth in claims 13 and 17 and methods of detecting E. coli using said nucleic acids as probes, does not reasonably provide enablement for any nucleic acid that encodes all or part of a flagellin protein with the expectation that the nucleic acid does not encode flagellin proteins expressed by E. coli H1, H7, H12 or H48 strains. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn broadly to any isolated nucleic acid encoding all or part of an E. coli nucleic acid molecule that encodes all or part of a flagellin protein, the molecule being capable of identifying an H serotype of E. coli, wherein the molecule does not encode a flagellin protein expressed by H1, H7, H12 or H48 type strains of E. coli. Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement". In the instant case, the specification has not taught a representative number of nucleic acids within the claimed genus and has not provided sufficient guidance as to how to obtain additional nucleic acids without undue experimentation. The specification teaches isolated nucleic acids consisting of SEQ ID NO: 1-68, wherein the nucleic acids encode a flagellin protein from one of the E. coli strains of H1, 2, 4-7, 9-12, 14-16, 18-21, 23-2, 26-34, 38, 39, 41-43, 45, 46, 49, 51, 52 and 56. The specification teaches comparing the sequences of SEQ ID NO: 1-68 in order to identify sequences that are specific for a given H serotype. However, the specification (page 2) also teaches that there are 4 loci in E. coli which encode for flagellin proteins, namely flk, fl1, flm, and fliC. The specification teaches that it is not

clear as to which loci some of the presently claimed nucleic acids have been obtained from. It is stated that "we have used the term "flagellin gene" in many cases where previously one would have used "fliC" to allow for the uncertainty as to the locus introduced by recent observations" (see page 13). The specification asserts that most E. coli strains express a single H antigen and thereby it is the nucleic acid molecule itself that is important and not the source of the nucleic acid. Regardless of the fact that most E. coli strains only express one flagellin gene, it appears that all E. coli strains contain each of the 4 flagellin loci. Yet, the specification has taught a single nucleic acid from each of the stated H types. The claims encompass nucleic acids from each of the loci of flk, fl1, flm and fliC from the 54 known H types of E. coli. While it is unclear as to which loci have been taught by the specification, it is clear that the specification has not taught a representative number of nucleic acids from each of the loci in each of the possible serotypes of E. coli. Furthermore, the specification demonstrates the unpredictability in obtaining the full length sequence of each of the flagellin genes in different E. coli H types. For example, at page 23, the specification states: "(f)or other strains, we were only able to amplify the flagellin gene using one or more of the other three pairs of primers, which are based on sequences within the *fliC* gene, and thus only partial sequence was obtained. These amplicons may be of the *fliC* gene or one of the alternative genes." At pages 26-28, the specification states that the full length flagellin genes from type strains H2, H3, H4, H5, H11, H17, H21, H24, H27, H29, H33, H38, H39, H42, and H56 have not been obtained. It is noted that the specification (page 24) states that the terminal regions of the flagellin gene are not important in determining antigenicity. However, the claims

are inclusive of full length flagellin gene sequences which are not taught in the specification and the specification has established the unpredictability in obtaining these full length sequences. The specification (page 3) also teaches that the flagellin gene sequences for H8 and H40 were identical. Accordingly, these sequences cannot be used to determine the specific H serotype of E. coli but can only be used to determine whether the E. coli is type H8 or H40. Further, the specification (page 40) states that "(o)ur work has shown that there are at least 7 cases where the H antigen type strains carry two antigen genes which appear to be complete and have the potential to function." The specification does not provide sufficient guidance as to how to obtain the flagellin genes from each of the 4 loci without undue experimentation. Further, the specification does not provide sufficient guidance as to how to distinguish between the nucleic acids from these loci and how to predictably identify subsequences within these as yet unisolated loci which are specific for an H serotype. As discussed by the specification the art of identifying and isolating the different flagellin genes from different loci is unpredictable. It is further unpredictable as to which sequences within these loci will be specific for a given H serotype. As taught in the specification (for example, page 31), some cross-reactivity with different strains is observed depending on the level of dilution of the anti-sera. For example, H11 cross reacts with anti-H21 and anti-H40. Accordingly, selection of subfragments of the flagellin gene that encode for type H specific antigens is unpredictable and can only be determined through experimentation. Additionally, the claims require that the nucleic acid does not encode a flagellin protein expressed by E. coli H1, H7, H12 or H48 type strains. Yet, the claims include SEQ ID NO: 66 which is

characterized in the specification (see for example page 16) as being specific for strain H1. The claims also include SEQ ID NO: 9 which is characterized as being specific for H7 and SEQ ID NO: 14 which is specific for H12. It is unpredictable as to how these sequences which are specific for H1, H7 and H12 can also not encode a protein expressed by E. coli H1, H7 or H12. Additionally, the claims (for example, claim 3) includes nucleic acids which include only a portion of SEQ ID NO: 1-68. The claims do not define the identity of the surrounding nucleotides and do not state the particular fragments of SEQ ID NO: 1-68 which would be required to provide the requisite attribute of allowing for the specific H serotype. The claims also include methods which use nucleic acids which hybridize to any gene encoding a transferase or a gene encoding an enzyme for the transport or processing of a polysaccharide unit, wherein the gene is involved in the synthesis of E. coli O antigen. Such nucleic acids are to be used to determine the O serotype of an E. coli strain. However, the specification teaches only the sequences set forth in claim 12 as being useful for determining the O serotype of E. coli strains. The claims thus include a huge genus of nucleic acids which are not disclosed in the specification, including nucleic acids from any gene encoding a transferase or a gene encoding an enzyme for the transport and processing of a polysaccharacride or oligonucleotide unit wherein the gene is involved in any manner with the synthesis of E. coli O antigen. For example, the claims may include genes rfc, rfbX, wbdM, wbdN, wbdO, wbdP, or wbdR or any other unstated gene having this functional activity but no specified structural properties. Adequate guidance has not been provided in the specification as to how to predictably identify additional nucleic acids useful for determining the O serotype of E.

coli without undue experimentation. Accordingly, in view of the lack of information in the specification as to how to reasonably identify other flagellin genes and genes useful for determining the O serotype of E. coli without undue experimentation and in view of the unpredictability in the art, the specification has not adequately taught one of skill in the art how to practice the claimed invention as it is broadly claimed.

5. Claims 1-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-31 are indefinite over the recitation of "capable of identifying" because capability is a latent characteristic and the claims do not set forth the criteria by which to determine capability. That is, it is not clear whether the recited nucleic acids have the potential to identify or do in fact specifically identify the H serotype of an E. coli. In the first instance, the claims do not set forth the conditions or types of assays under which the nucleic acids do in fact identify a H. serotype. It is also unclear as to what is meant by a nucleic acid that identifies a serotype. While it is clear as to what is meant by a nucleic acid that specifically hybridizes to a given H serotype of E. coli, it is unclear as to what is meant by the nucleic acid itself identifying a serotype.

Claims 6 and 31 are indefinite and confusing because the claim does not clearly set forth what constitutes the group from which the primers are selected. The claim includes a table which lists "Positions of primer 1" and "Positions of primer 2". The position of a primer is distinct from

the primer itself. Since the table does not specifically refer to individual primers, it is unclear as to what primer constitute the group of primers set forth in the "table above."

Claims 7-21 and 26-29 are indefinite over the recitation of "detecting the H serotype of E. coli" and "detecting the H and O serotype of E. coli." It is not clear as to whether the claims encompass detecting the presence of an E. coli which has an H and/or O serotype or if the claims require determining the H or O serotype of an E. coli present in a sample (i..e, characterizing an E. coli based on whether it's serotype is H1, H2, H3 etc).

Claims 7 and 8 are indefinite because the claims refer to a step of "detecting **a** nucleic acid molecule which is hybridized to the gene." However, the claims do not clarify as to whether this nucleic acid is the same or different from the nucleic of step (a). Similarly, claims 9 and 10 are indefinite over the recitation of "detecting a pair of nucleic acid molecules."

Claims 9, 10, 26, 27 are indefinite over the recitation of "a pair of nucleic acid molecules according to claim 1" because this phrase lacks proper antecedent basis. While claim 1 refers to a nucleic acid molecule, it does not refer to a pair of nucleic acid molecules.

Claims 11-14 are indefinite over the recitation of "the nucleic acid molecule to hybridise to the gene" (see step b) because it is not clear as to whether this refers to the nucleic acid molecule derived from a gene encoding a transferase or the nucleic acid molecule according to claim 1. Similarly, the claims are indefinite over the recitation of "detecting the nucleic acid molecules which are hybridised to the genes" because it is not clear as to whether this refers to the nucleic acids and genes of (a), the nucleic acids and genes of (b), or both. Similarly, claims 15-18 are

indefinite and confusing over the recitations of "the pair of nucleic acid molecules" (in step (b)) and "detecting pairs of nucleic acid molecules which are hybridised to the genes."

Claim 13 is indefinite and confusing because it is not clear as to whether the primers consist of the specified nucleotides of SEQ ID NO: 1 or 2 or if these are the nucleotide positions in SEQ ID NO: 1 and 2 and the primers consist of these corresponding sequences from, e..g, SEQ ID NO: 56. It is unclear as to what is intended to be the relationship between the nucleic acids of claim 13 and those recited in claim 12. It is similarly unclear as to what constitutes the primers set forth in claims 17 and 25 and as to whether the primers consist of or comprise the stated sequence (e.g., does the primer consist of nucleotides 739-757 of SEQ ID NO: 1 or 56 or comprise nucleotides 739-757 of SEQ ID NO: 1 or 56).

Claims 19-21 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. The claims require detecting the H and O serotype. Yet, the claims recite a single step of contacting an E. coli gene with a nucleic acid molecule that "identifies" an H serotype. The claims do not clarify how this step results in the determination of the O serotype. See MPEP § 2172.01.

Claim 24-25 are indefinite and confusing because it is not clear as to whether the nucleic acid consists of or comprises or is derived from (and thereby may have any level of sequence identity with) , for example, nucleotides 739-1932 of SEQ ID NO: 45. The claims are particularly

confusing in view of the fact that claim 25 is limited to specific subfragments of the sequences set forth in claim 24.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Fields (Journal of Clinical Microbiology. May 1997. 35: 1066-1070).

Fields (see, for example, page 1067 and Figure 1) teaches PCR amplification of the fliC gene of different H serotypes of E. coli, including the serotypes H5, H29, H56, H36, H53, H51, and H44. These nucleic acids have distinct nucleotide sequences and the differences in their nucleotide sequences could be used to distinguish between these H serotypes of E. coli. Accordingly, Fields teaches isolated nucleic acids which encode at least a portion of an E. coli flagellin (fliC) protein, wherein the nucleic acid is capable of identifying an H serotype of E. coli when hybridized to an E. coli nucleic acid that encodes a flagellin protein and wherein said nucleic acid does not encode a flagellin protein expressed by E. coli H1, H7, H12, or H48 type strains. Since the H serotypes set forth by Fields are of the same E. coli H types containing the nucleic acids of SEQ ID NO: 7, 28, 54, and 50, it is a property of the nucleic acids of Fields that they contain a least a part of these nucleic acids. Further, Fields (page 1067) teaches 2 nucleic

acid primers, one of 25 nucleotides and one of 20 nucleotides (which is considered to be encompassed by "about 10 to 20 nucleotides in length") wherein the primers are capable of identifying an H serotype since the primers can be used to amplify E. coli fliC H serotypes and the amplified nucleic acids can be used to distinguish between the H serotypes.

7. Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Ratiner (reference 'A6'; Journal of Bacteriology (Feb 1998) 180:979-984).

Ratiner teaches an isolated nucleic acid encoding the E. coli flagellin FlA and flmA genes from serotypes H44, H54 and H55 (see, for example, page 979). These nucleic acids have a distinct nucleotide sequence as compared to the nucleotide sequence of other H serotypes and these differences in the nucleotide sequence could be used to distinguish between these H serotypes of E. coli. Accordingly, Ratiner teaches an isolated nucleic acid which encodes at least a portion of an E. coli flagellin protein , wherein the nucleic acid is capable of identifying an H serotype of E. coli when hybridized to an E. coli nucleic acid that encodes a flagellin protein and wherein said nucleic acid does not encode a flagellin protein expressed by E. coli H1, H7, H12, or H48 type strains. With respect to claim 3, the claims include nucleic acids which comprise any portion of any length of SEQ ID NO: 1-68. Since the flagellin nucleic acids share some level of sequence identity, the nucleic acids of Ratiner have the property of comprising a least a portion of SEQ ID NO: 1-68.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fields in view of Ahren (The Scientist. July 1995. 19 (155): 20-24).

Fields (see, for example, page 1067 and Figure 1) teaches PCR amplification of the fliC gene of different H serotypes of E. coli, including the serotypes H5, H29, H56, H36, H53, H51, and H44. These nucleic acids have distinct nucleotide sequences and the differences in their nucleotide sequences could be used to distinguish between these H serotypes of E. coli. Accordingly, Fields teaches isolated nucleic acids which encode at least a portion of an E. coli flagellin (fliC) protein, wherein the nucleic acid is capable of identifying an H serotype of E. coli when hybridized to an E. coli nucleic acid that encodes a flagellin protein and wherein said nucleic acid does not encode a flagellin protein expressed by E. coli H1, H7, H12, or H48 type strains. Since the H serotypes set forth by Fields are of the same E. coli H types containing the

nucleic acids of SEQ ID NO: 7, 28, 54, and 50, it is a property of the nucleic acids of Fields that they contain a least a part of these nucleic acids. Further, Fields (page 1067) teaches 2 nucleic acid primers, one of 25 nucleotides and one of 20 nucleotides (which is considered to be encompassed by "about 10 to 20 nucleotides in length") wherein the primers are capable of identifying an H serotype since the primers can be used to amplify E. coli fliC H serotypes and the amplified nucleic acids can be used to distinguish between the H serotypes. Fields does not teach packaging the nucleic acids in kits.

However, reagent kits for performing DNA detection assays were conventional in the field of molecular biology at the time the invention was made. In particular, Ahren discloses the general concept of kits for performing nucleic acid detection methods and discloses that kits provide the advantage of pre-assembling the specific reagents required to perform an assay and ensure the quality and compatibility of the reagents to be used in the assay and allows investigators to save time and money (see for example page 23). Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the nucleic acids of Fields in a kit for the expected benefits of convenience and cost-effectiveness for practioners of the art wishing to amplify fliC genes or wishing to use fliC nucleic acids as probes to characterize and detect E. coli H serotypes.

9. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ratiner in view of Ahren.

Ratiner teaches an isolated nucleic acid encoding the E. coli flagellin FlA and flmA genes from serotypes H44, H54 and H55 (see, for example, page 979). These nucleic acids have a distinct nucleotide sequence as compared to the nucleotide sequence of other H serotypes and these differences in the nucleotide sequence could be used to distinguish between these H serotypes of E. coli. Accordingly, Ratiner teaches an isolated nucleic acid which encodes at least a portion of an E. coli flagellin protein , wherein the nucleic acid is capable of identifying an H serotype of E. coli when hybridized to an E. coli nucleic acid that encodes a flagellin protein and wherein said nucleic acid does not encode a flagellin protein expressed by E. coli H1, H7, H12, or H48 type strains. Ratiner teaches the use of these nucleic acids to further characterize the E. coli H serotypes. Ratiner does not teach packaging the nucleic acids in a kit.

However, reagent kits for performing DNA detection assays were conventional in the field of molecular biology at the time the invention was made. In particular, Ahren discloses the general concept of kits for performing nucleic acid detection methods and discloses that kits provide the advantage of pre-assembling the specific reagents required to perform an assay and ensure the quality and compatibility of the reagents to be used in the assay and allows investigators to save time and money (see for example page 23). Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the nucleic acids of Ratiner in a kit for the expected benefits of convenience and cost-effectiveness for practioners of the art wishing to characterize and detect E. coli H serotypes.

10. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fields in view of Ahren and further in view of Stevenson (reference 'B5'; Journal of Bacteriology. 1994. 176: 4144-4156).

The teachings of Fields and Ahren are presented above. In particular, Fields teaches the analysis of the *fliC* gene and teaches *fliC* nucleic acids. Fields also teaches that the presently disclosed PCR-RFLP analysis in conjunction with O serotype analysis will be useful in identifying E. coli strains. Fields and Ahren do not teach packaging both *fliC* nucleic acids and nucleic acids encoding a gene for the O antigen in a kit.

However, Stevenson teaches nucleic acids encoding rfb, which is a gene involved in the synthesis of the E. coli O antigen. Stevenson (page 4147 and 4153) also teaches DNA hybridization methods for detecting E. coli O antigens.

In view of the teachings of Stevenson, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have included the nucleic acids of Stevenson in the kit containing *fliC* nucleic acids in order to have provided a convenient and cost-effective kit useful for practioners in the art wishing to characterize and detect E. coli H and O serotypes.

11. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ratiner in view of Ahren and further in view of Stevenson (reference 'B5'; Journal of Bacteriology. 1994. 176: 4144-4156).

The teachings of Ratiner and Ahren are presented above. In particular, Ratiner teaches flagellin *flA* and *flmA* nucleic acids of E. coli serotypes H44, H54 and H55 and the analysis of

these nucleic acids. The combined references do not teach packaging both flagellin nucleic acids and nucleic acids encoding a gene for the O antigen in a kit.

However, Stevenson teaches nucleic acids encoding rfb, which is a gene involved in the synthesis of the E. coli O antigen. Stevenson (page 4147 and 4153) also teaches DNA hybridization methods for detecting E. coli O antigens.

In view of the teachings of Stevenson, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have included the nucleic acids of Stevenson in the kit containing flagellin nucleic acids in order to have provided a convenient and cost-effective kit useful for practioners in the art wishing to characterize and detect E. coli H and O serotypes.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (703) 308-2199. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703)-308-1119. Papers related to this application may be faxed to Group 1634 via the PTO Fax Center using the fax number (703)-872-9306 or (703)-872-9307 (after final).

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Carla Myers

June 30, 2003

CARLA J. MYERS
PRIMARY EXAMINER